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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
GAKH, YELENA G	

ART UNIT	PAPER NUMBER
1797	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/533,420	CHEN ET AL.	
	Examiner	Art Unit	
	Yelena G. Gakh, Ph.D.	1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 March 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6 and 24-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 24-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Amendment filed on 03/23/09, is acknowledged. New claims 24-35 are added. Thus, claims 1-6 and 24-35 are pending in the application and are considered on merits.

Response to Amendment

2. The amendment filed 03/23/09 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: the recitations of claims 27-35. In the originally field application the combinations were recited in claim 2 as optional embodiments, which were not supported by the specification.

Applicant is required to cancel the new matter in the reply to this Office Action.

3. In response to the amendment the examiner modifies rejection of the claims under the second paragraph of 35 U.S.C. 112. The examiner maintains the rejection of claims 1-6 as being anticipated by Cima and establishes rejection of claims 24-35 as being obvious over Cima.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 26-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 26 recites adding a solvent in step (iii) and adding a solvent in step (iv). It is not apparent, whether it is the same solvent, or these are two different solvents, which is essential for performing the method recited in claim 26. The examiner considers this as the same solvent.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. **Claims 1-6 and 24-25** are rejected under 35 U.S.C. 102(e) as being anticipated by Cima et al. (US 2002/0048610 A1) or .

Cima teaches "high-throughput formation, identification, and analysis of diverse solid forms" (Title), high-throughput formation comprising dissolving drug candidates in various solvents, adding different additives and subjecting libraries under various crystallization conditions, including determining solubility of different polymorphs. Specifically, the subject matter of claims 1-6 is covered by the following paragraphs in Cima's disclosure:

> "[0002] This invention is directed to the generation and processing of data derived from large numbers of samples, the samples comprising crystalline, amorphous, and other forms of solid substances, including chemical compounds. More specifically, the invention is directed to methods and systems for rapidly producing and screening large numbers of samples to detect the presence or absence of solid-forms. **The invention is suited for discovering: (1) new solid-forms with beneficial properties and conditions for their formation, (2) conditions and/or compositions affecting the structural and/or chemical stability of solid-forms, (3) conditions and/or compositions that inhibit the formation of solid-forms; and (4) conditions and/or compositions that promote dissolution of solid-forms**".

> "[0032] In one embodiment, the invention relates to arrays comprising 2 or more samples, for example, about 24, 48, 96, to hundreds, thousands, ten thousands, to hundreds of thousands or more samples, one or more of the samples comprising solid-forms in gram, milligram, **microgram, or nanogram** quantities and practical and cost-effective methods to rapidly produce and screen such samples in parallel. *These methods provide an extremely powerful tool for the rapid and systematic analysis, optimization, selection, or discovery of conditions, compounds, or compositions that induce, inhibit, prevent, or reverse formation of solid-forms.* For example, the invention provides methods for systematic analysis, optimization, selection, or discovery of novel or otherwise beneficial solid-forms (e.g., beneficial pharmaceutical solid-forms having desired properties, such as improved bioavailability, solubility, stability, delivery, or processing and manufacturing characteristics) and conditions for formation thereof. The invention can also be used to identify those conditions where high-surface-area crystals or amorphous solids are prepared (e.g., nanoparticles) directly by precipitation or crystallization thus obviating the step of milling.
> [0033] In another embodiment, the invention is useful to discover solid forms that posses preferred **dissolution** properties. In this embodiment, arrays of solid forms of the compound-of-interest are prepared. Each element of the array is prepared from different solvent and additive combinations with differing process histories. **The solids are separated from any liquid that**

> **may be present. In this way, one has obtained an array of solid forms of the compound-of-interest. One then adds, to each sample of the array, the same dissolution medium of interest.** Thus, one would add simulated gastric fluid if the application if to optimize the dissolution of drug substance in oral dosage forms. **The dissolution medium of each array element is then sampled versus time to determine the dissolution profile of each solid form.** Optimum solid forms are ones where dissolution is rapid and/or that the resulting solution is sufficiently metastable so as to be useful. Alternatively, one may be interested in solid forms that dissolve at a specified rate. Examination of the multitude of dissolution profiles will lead to the optimum solid form."

> "[0139] Sub-arrays or even individual samples within an array can be subjected to processing parameters that are different from the processing parameters to which other sub-arrays or samples, within the same array, are subjected. Processing parameters will differ between sub-arrays or samples when they are intentionally varied to induce a measurable change in the sample's properties. Thus, according to the invention, minor variations, such as those introduced by slight adjustment errors, are not considered intentionally varied."

Thus, Cima teaches the method for determining how the solubility (Claims 1, 2), dissolution (Claims 3, 4), or stability (Claims 5, 6) of polymorphs depend on the solid form by preparing an array of samples with a controlled amount of the compounds-of-interest in micrograms or nanograms quantity (which is less than 100 μg), forming a liquid portion by adding a solvent and determining how much compound-of interest is dissolved in the liquid portion depending on its form. For dissolution measurements "the dissolution medium of each array element is then sampled versus time to determine the dissolution profile of each solid form." "Examination of the multitude of dissolution profiles will lead to the optimum solid form."

Regarding stability of the various polymorphs Cima discloses the following:

> "[0145] Physical properties include, but are not limited to, **physical stability**, melting point, solubility, strength, hardness, compressibility, and compactability. Physical stability refers to a compound's or composition's ability to maintain its physical form, for example maintaining particle size; maintaining crystal or amorphous form; maintaining complexed form, such as hydrates and solvates; resistance to absorption of ambient moisture; and maintaining of mechanical properties, such as compressibility and flow characteristics. Methods for measuring physical stability include spectroscopy, sieving or testing, microscopy, sedimentation, stream scanning, and light scattering. **Polymorphic changes, for example, are usually detected by differential scanning calorimetry or quantitative infrared analysis.** For a discussion of the theory and methods of measuring physical stability see Fiese et al., in The Theory and Practice of Industrial Pharmacy, 3rd ed., Lachman L.; Lieberman, H. A.; and Kanig, J. L. Eds., Lea and Febiger, Philadelphia, 1986 pp. 193-194 and Remington 's Pharmaceutical Sciences, 18th Edition, ed. Alfonso Gennaro, Mack Publishing Co. Easton, Pa., 1995, pp. 1448-1451, both of which are incorporated herein by reference."

To the examiner's understanding Cima's disclosure covers the subject matter of the indicated claims.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. **Claims 24-35** are rejected under 35 U.S.C. 103(a) as being unpatentable over Cima.

As has been indicated previously regarding dissolution of the solid forms, Cima discloses the following:

> [0033] In another embodiment, the invention is useful to discover solid forms that posses preferred **dissolution** properties. In this embodiment, arrays of solid forms of the compound-of-interest are prepared. Each element of the array is prepared from different solvent and additive combinations with differing process histories. **The solids are separated from any liquid that may be present. In this way, one has obtained an array of solid forms of the compound-of-**

> **interest. One then adds, to each sample of the array, the same dissolution medium of interest.** Thus, one would add simulated gastric fluid if the application if to optimize the dissolution of drug substance in oral dosage forms. **The dissolution medium of each array element is then sampled versus time to determine the dissolution profile of each solid form.** Optimum solid forms are ones where dissolution is rapid and/or that the resulting solution is sufficiently metastable so as to be useful. Alternatively, one may be interested in solid forms that dissolve at a specified rate. Examination of the multitude of dissolution profiles will lead to the optimum solid form."

Thus, Cima discloses sampling the dissolution medium of each array element versus time. It is equivalent to forming an array of samples of the same quantities and measuring dissolution rate not for the same sample, but for the array of samples dissolved in the same aliquots of the solvent and determining the dissolution profile by separating the liquid portion of each sample at a different time point. Therefore, it would have been obvious for a person of ordinary skill in the art to replace measurement of the dissolved form in the same sample at certain time intervals with an equivalent measurement of the dissolved form in the array of equivalent samples at certain time point for each sample, because this yields the same result and is more convenient. The various forms recited in claims 27-35 are all variants disclosed by Cima.

Response to Arguments

12. Applicant's arguments filed 03/23/09 have been fully considered but they are not persuasive.

Regarding rejection of claims 1-6 as being anticipated by Cima, the examiner is not quite sure, as to how Cima's disclosure is different from the claimed invention. Cima specifically discloses preparing an array of samples in different physical and/or chemical forms and determining, how different physical and/or chemical forms affect the compounds' solubility and dissolution property.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yelena G. Gakh, Ph.D. whose telephone number is (571) 272-1257. The examiner can normally be reached on 9:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Vickie Y. Kim can be reached on (571) 272-0579. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Yelena G. Gakh/
Primary Examiner, Art Unit 1797

5/10/2009